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Externalization of neuronal somata as an evolutionary strategy for energy economization

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Neuronal morphology of vertebrates and many invertebrates differs in a fundamental aspect: the location of neuronal cell bodies (somata) relative to their dendritic and axonal trees. The somata of most vertebrate neurons are located centrally between dendrites and axon. In contrast, neurons of various invertebrates, such as arthropods and cephalopods, typically externalize their somata to the end of a single process called a 'stem neurite' (Figure 1A). While this difference has been related to advantages of a spatial separation of neuropil and externalized somata [1–5], we here propose that the right soma location also reduces signal attenuation and consequently the energetic cost of signaling. Neurons commonly transfer signals from their dendrites to the axon, such that signals depolarize a centrally located soma before reaching the axon. The signal attenuation resulting from leakage through the soma membrane can be decreased through externalization of the soma, resulting in a reduction of the depolarized membrane area. In the light of evolutionary pressure towards energy-efficient signaling [6,7], we argue that an externalization of the soma is advantageous for relatively large somata. We support this hypothesis on the basis of compartmental models and previously published experimental data.

Typically, synaptic inputs depolarize the neuronal membrane. This signal propagates from the dendrites to the axon, where a spike can be initiated. On the way, depolarization amplitude is attenuated by passive properties of the membrane — a process that is counteracted by active membrane properties, such as voltage-activated sodium conductances. The lower the passive attenuation, the lower the amount of metabolic energy that needs to be invested in its compensation (either by boosting of the signal via active membrane properties or a larger synaptic input [8,9]). We here suggest that the right soma location decreases passive signal attenuation and hence also metabolic cost.

For a 'central soma' located between dendrites and axon, passive signal attenuation increases with the size of the soma membrane surface. A relocation of the soma to the end of a stem neurite (an 'externalized soma') removes the soma membrane from the signaling path (Figure 1A). Instead, signal attenuation occurs at the additional membrane provided by the stem neurite. An efficient soma location must therefore respect the trade-off between (central) soma surface and extra surface provided by the stem neurite.

In simulations of multicompartmental models with different soma locations and otherwise identical parameters (Figure S1A in Supplemental Information, published with this article online), we quantified the signal attenuation by the minimal dendritic signal amplitude required to reach a target depolarization in the axon (a spike, or, for passive models, a voltage threshold). The smaller this minimal dendritic signal, the smaller the signal attenuation between dendrites and axon. We show that the ratio of signal attenuation between models with central and externalized somata increases with the 'soma-to-neurite ratio', i.e., the ratio of the soma surface A and the 'depolarized' stem neurite surface, $A/\pi d\lambda$. The latter ratio depends on both morphological and electrophysiological parameters (see Supplemental Information). The critical soma-to-neurite ratio, defined as the value where attenuation in both models is equal, increases slightly with signal duration (Figure 1C, dashed curve). The simulations agree with corresponding analytical calculations (Figure 1C, solid curve). The calculations demonstrate that for short stimuli, externalized somata yield larger voltage responses than central somata (Figure 1B). All

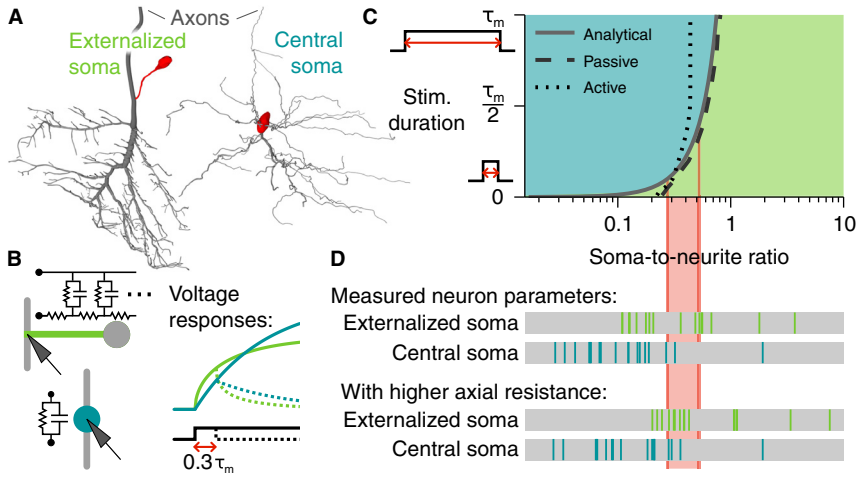

Figure 1. Signal attenuation in neurons with central or externalized soma location.
(A) Distinct morphology of neurons in the central nervous system of various invertebrates and vertebrates: in the former, the soma is externalized, while in the latter, a central location of the soma predominates (examples from blowfly and rat). (B) Left: circuit diagrams representing the analytical, simplified models. Right: voltage response to injected current pulses. The build-up of depolarization is initially faster for externalized somata, rendering them well adapted for the transmission of brief stimuli or high frequencies. (C) Color-coded morphology (either externalized in green, or central in blue) that is advantageous for signal attenuation as a function of the stimulus duration and the soma-to-neurite ratio for passive analytical models. Curves depict the critical soma-to-neurite ratios: analytical solution (solid curve), multicompartmental models with purely passive conductances (dashed), active models including spike generation (dotted). Above the critical soma-to-neurite ratio, externalization enhances energy efficiency. For illustration, the red box marks the soma-to-neurite interval corresponding to a biologically relevant range of stimulus durations ($0.1\tau_m$ – $0.4\tau_m$). (D) Experimental data on the soma-to-neurite ratio for neurons from various species (each vertical bar corresponding to one cell type; for details see Supplemental Information). Top: based on axial resistances as measured in dendrites or axons of the respective neurons, average soma-to-neurite ratio is larger in cells with externalized soma than in those with central soma. Bottom: assuming a higher axial resistance in the stem neurite (model prediction) increases this trend.

results qualitatively hold for models including active (Hodgkin–Huxley type) conductances in the axon (Figure 1C, dotted curve).

In summary, externalization of the soma reduces signal attenuation in cases of a large soma, a thin stem neurite, or a leaky membrane. Consequently, we predict that neurons with externalized soma tend to have a high soma-to-neurite ratio. For neurons with central soma, the soma-to-neurite ratio is not defined. Still, we can ask whether the central soma location would be more energy efficient, if the alternative was to move the soma to the end of a neurite whose diameter is assumed to scale with the diameter of the cell's proximal dendrites. Thus defining a soma-to-neurite ratio based on a 'virtual' stem neurite for neurons with central soma, we evaluate previously published morphological and electrophysiological data from various species and cell types (Table S1). Indeed, the soma-to-neurite ratio is significantly larger for neurons with externalized soma compared to neurons with central soma (Figure 1D, top traces, directed Mann-Whitney-U test with $p < 0.01$).

The soma-to-neurite ratio also depends on the length constant λ of the stem neurite, and hence on its axial resistance (see Supplemental Information). Experimental values of the latter were mostly derived from axons, where a low axial resistance facilitates signal propagation. A higher axial resistance in the stem neurite, however, would shield the soma and thus reduce signal attenuation. Based on our analysis, we hence predict that axial resistance in the stem neurite should be larger than in the axon. Assuming a higher, yet biologically plausible, axial resistance for the calculation of the soma-to-neurite ratio (250 Ωcm^2) allows for a better separation of soma-to-neurite ratios between central and externalized neurons (Figure 1D, bottom traces), in quantitative agreement with the optimal morphologies derived from the model (Figure 1C). This prediction on an electrophysiological parameter distinguishes our study from approaches based entirely on morphological aspects, and can be tested experimentally.

Our results suggest that an externalization of large somata decreases signal attenuation between dendrites and axon, benefiting information transfer in the context of noise, and saving metabolic energy otherwise required for an active boosting of neuronal signals. Previous work emphasized advantages of an externalization of the soma to the ganglion surface in the context of a separation of neuropil and soma layer, i.e., wiring length minimization [1,4], the use of graded potentials [5], and somatic access to nutrients [2,3]. Externalization has been proposed to shorten conduction times [1], which is a trend that is also found in our models. Our analysis adds a new perspective to the differential evolution of neuronal morphologies based on considerations of energy efficiency and reduced signal attenuation. While these effects hold for signals of different durations, quantitatively, externalization of the soma is particularly advantageous if inputs are short (Figure 1C).

Whether externalized somata of large size or central somata of small size — relative to the neurites — are favorable, is likely to be determined by additional factors. Those include constraints on the axial resistance of the stem neurite, the required soma volume for maintenance of the cell (such as for the synthesis machinery), the need for a central point of action for recurrent connections, and the frequency content of inputs.

It is noteworthy that even in mammals there are exceptions to the central soma location. Dorsal root ganglion cells transmit information from peripheral sensory areas along the spinal cord to the brain. These neurons exhibit large, externalized somata attached to stem neurites, the latter of which oftentimes are artificially prolonged by extensive wrapping around the soma [10]. We argue that this externalized morphology matches neuronal function: a central action point for recurrent connections is not required, somata can be larger to meet the maintenance demands of these extended cells, and a long stem neurite facilitates transmission of short signals (i.e., action potentials).

Interestingly, a look at the phylogenetic tree suggests that the Ur-bilaterian did not show an extensive externalization of neuronal somata (see Supplemental Information). Externalization of somata in higher invertebrates may hence have constituted an evolutionary strategy reducing neuronal energy consumption and signal attenuation while allowing for larger soma sizes (potentially desirable to accommodate more synthesis machinery for progressively elaborate nervous systems). Vertebrate neurons with central soma morphology may, on the other hand, have been preserved due to additional constraints and alternative optimization strategies, potentially including a higher recurrent connectivity or the outsourcing of organelles from soma into proximal dendrites.

SUPPLEMENTAL INFORMATION

Supplemental Information contains methods, one figure, and one table and can be found with this article online at http://dx.doi.org/10.1016/j.cub.2015.02.024.

REFERENCES

1. Ramón y Cajal, S. (1999). Texture of the Nervous System of Man and the Vertebrates, Volume I, P. Pasik and T. Pasik, eds. (New York: Springer).
2. Hanström, B. (1928). Some points on the phylogeny of nerve cells and of the central nervous system of invertebrates. J. Comp. Neurol. *46*, 475–493.
3. Sánchez-Soriano, N., Bottenberg, W., Fiala, A., Haessler, U., Kerassoviti, A., Knust, E., Löhr, R., and Prokop, A. (2005). Are dendrites in Drosophila homologous to vertebrate dendrites? Dev. Biol. *288*, 126–138.
4. Rivera-Alba, M., Peng, H., de Polavieja, G.G., and Chklovskii, D.B. (2014). Wiring economy can account for cell body placement across species and brain areas. Curr. Biol. *24*, R109–R110.
5. Niven, J.E., and Farris, S.M. (2012). Miniaturization of nervous systems and neurons. Curr. Biol. *22*, R323–R329.
6. Laughlin, S.B., and Sejnowski, T.J. (2003). Communication in neuronal networks. Science *301*, 1870–1874.
7. Niven, J.E., and Laughlin, S.B. (2008). Energy limitation as a selective pressure on the evolution of sensory systems. J. Exp. Biol. *211*, 1792–1804.
8. Attwell, D., and Laughlin, S.B. (2001). An energy budget for signaling in the grey matter of the brain. J. Cereb. Blood Flow Metab. *21*, 1133–1145.
9. Sengupta, B., Stemmler, M., Laughlin, S.B., and Niven, J.E. (2010). Action potential energy efficiency varies among neuron types in vertebrates and invertebrates. PLoS Comput. Biol. *6*, e1000840.
10. Matsuda, S., Kobayashi, N., Terashita, T., Shimokawa, T., Shigemoto, K., Mominoki, K., Wakisaka, H., Saito, S., Miyawaki, K., Saito, K., *et al*. (2005). Phylogenetic investigation of Dogiel's pericellular nests and Cajal's initial glomeruli in the dorsal root ganglion. J. Comp. Neurol. *491*, 234–245.

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